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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,747	06/24/2003	Laura A. Bedzyk	CL1686USDIV	9974

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EXAMINER

MARVICH, MARIA

ART UNIT PAPER NUMBER

1636

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/602,747

Applicant(s)

BEDZYK ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 8, 9 and 14-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 8, 9 and 14-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to amendment filed 10/20/04. Claims 5-7, 10-13 and 17-28 have been cancelled. Claims 1, 2, 4, 8 and 14-16 have been amended. Claims 1-4, 8, 9 and 14-16 are pending in the application.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are new grounds of rejection herein that were not necessitated by applicants' amendment and therefore, this action is not final.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Priority

In the reference to the prior application inserted, as the first sentence of the specification of this application, the current status of all nonprovisional parent applications referenced should be updated. Specifically, U.S. Serial No. 09/891,641, filed June 26, 2001, is now U.S. Patent No. 6,617,148. Furthermore, the status of the provisional applications 60/214,967 and 60/268,320 is incorrectly indicated as expired, which is technically incorrect. As the applications are not patents, they are not subject to expiration.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 8 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

The instant claims recite a method for the expression of a coding sequence using a promoter region of a *Bacillus* sp. *yvaWXY* gene.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, the specification teaches the identification of genes that are expressed in response to stimuli such as oxygen depletion. The promoter that drives expression of the *Bacillus subtilis* *yvaWXY* gene was identified by high throughput analysis of genes induced upon oxygen depletion (page 18, line 16-19). The nucleotide sequence of *yvaWXY* of *Bacillus subtilis* is contained in SEQ ID NOs 8, 9 and 10. Applicants state that homologs of the genes can be

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identified. However, applicants do not disclose any homologues of *yvaWXY* gene or promoters from other species of *Bacillus*. Applicants have not reduced to practice the claimed invention. SEQ ID NO:8 did not correspond to any sequences in the art based upon a sequence search against patent and non-patent literature, other than for the *yvaWXY* gene promoter from *Bacillus subtilis*. While applicants have disclosed the sequence of SEQ ID NO:8, and provided the hybridization conditions that might lead to identification of homologues, applicants have not described the structural features of the *Bacillus subtilis yvaWXY* gene required for its activity or whether such structural/functional characteristics are conserved across *Bacillus subtilis*. For example, applicants have not provided a correlation between the structure of *yvaWXY* and the ability of its promoter to drive expression under conditions of oxygen depletion. Given the large genus of genes from all *Bacillus* species encompassed by the rejected claims, the uncertainty of identifying homologues and the uncertainty of the activity of any of the gene promoters to correspond to that of the *Bacillus subtilis yvaWXY* promoter to be effective in driving gene expression as recited, it must be considered that any promoter must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claims 1-3, 8 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of expressing a coding region of interest using the promoter of SEQ ID NO:8, *Bacillus subtilis yvaWXY* promoter does not reasonably provide enablement for use of any promoter from any *Bacillus yvaWXY* gene. The specification does not

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enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. **This is a new rejection.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention.** The invention recites a method for the expression of a chimeric gene comprised of a promoter and a coding sequence. cDNA microarray techniques that allow identification of genes that are differentially regulated under various stresses and environmental conditions were used to identify promoters to be used for protein production at stationary phase such as the promoter driving expression of the *yvaWXY* gene obtained from *Bacillus subtilis*. The instant invention utilizes disciplines of molecular biology and cell culture.

2) **Scope of the invention.** The claims recite that the coding sequence is linked to the promoter region of a *Bacillus yvaWXY* gene. However, applicants only disclose the promoter from the *yvaW* of *Bacillus subtilis*, which is disclosed as SEQ ID NO:8 and contains the promoter. Applicants do not provide sufficient guidance to determine the particular members of the large genus of promoters encompassed by the rejected claims.

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3) Number of working examples and guidance. Applicants have disclosed the sequence of SEQ ID NO:8, which corresponds to *yvaWXY* of *Bacillus subtilis*. Furthermore, applicants provided hybridization conditions that might lead to identification of homologues and state that the genes can be identified in homologues.

4) State of Art. Previously, *Bacillus* was thought to only grown in aerobic conditions (Nakano et al, 1997; applicant provided). Identification and characterization of anaerobic growth pathway in *Bacillus* has revealed several genes that are involved in anaerobic growth conditions. Subsequently it was found that in aerobic growth conditions, cells grow increasing biomass. Upon entry of stationary phase, the cells can be induced to produce protein by induction of genes associated with increased expression upon anaerobic conditions or stationary growth phase. Traditionally, *E. coli* cells have been used for large-scale production of proteins. Isolation and characterization of *yvaWXY* was previously unknown in the art and therefore, methods for its use in protein production are unknown. SEQ ID NO:8 did not correspond to any sequences in the art based upon a sequence search against patent and non-patent literature other than for the *yvaWXY* gene promoter from *Bacillus subtilis*.

5) Unpredictability of the art. The art of the instant invention is basically predictable as most components of the invention are built upon well-developed skills. For example, high throughput screening for the identification of genes induced in response to stimuli, protein production in *Bacillus*, cloning of promoters and coding regions are well developed skills of the art. However, the ability to use the instant invention is highly unpredictable for any promoter from any *Bacillus* sp. *yvaWXY* gene given the lack of disclosure of the recited promoters. Furthermore, applicants provide little guidance for the isolation of the proper promoter and the

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ability to determine *a priori* that a homologue has a promoter that functions as recited is not a high art.

6) **Summary.** The invention recites a method for the expression of a chimeric gene comprised of a promoter and a coding sequence. The unpredictability of using the claimed invention for any promoter from any *Bacillus* sp. *yvaWXY* gene is high.

In view of predictability of the art to which the invention pertains and the lack of: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 8-9, 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claim 2 is vague and indefinite in that the metes and bounds of “removing oxygen from the transformed *Bacillus* sp. cell of step (b) whereby the chimeric gene is expressed” are unclear. The specification teaches that the protein is expressed in the absence of oxygen only in the log phase whereas at stationary phase, protein is expressed in the presence of oxygen. In claim 2, it is

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unclear if the cells have reached stationary phase or are in log phase. If the cells have reached stationary phase it is unclear how the protein is expressed. If the cells are only in log phase, it would be remedial to recite that.

Claim 3 is vague and indefinite in that the metes and bounds of "oxygen is re-supplied to the transformed *Bacillus* sp. cell" are unclear. It is unclear if this step is also intended for protein expression as in claim 2 or for some other outcome such as bioconversion.

Claim 8 is vague and indefinite in that the metes and bounds of "about T0" are unclear. The term "about" is a relative one not defined by the claim, no single set of conditions is recognized by the art as being "" and because the specification does not provide a standard for ascertaining the requisite degree, the metes and bounds of this claim cannot be established

Conclusion

Claims 1-4, 8-9 and 14-16 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

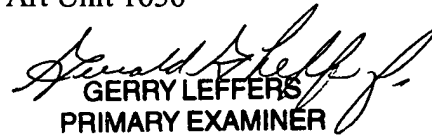
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

January 5, 2004


GERRY LEFFERS
PRIMARY EXAMINER